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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/553,262	12/20/2005	David Rubinsztein	BJS-620-394	1781

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EXAMINER	
ZAREK, PAUL E	

ART UNIT	PAPER NUMBER
1628	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/553,262	RUBINSZTEIN ET AL.	
	Examiner	Art Unit	
	Paul Zarek	1628	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 November 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *41 and 43-93* is/are pending in the application.

4a) Of the above claim(s) *52-93* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *41 and 43-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claim 41 has been amended and Claim 42 has been cancelled by the Applicants in correspondence filed on 11/23/2009. Claims 41 and 43-93 are currently pending. Claims 52-93 remain withdrawn as being drawn to nonelected subject matter. This is the second Office Action on the merits of the claim(s).

RESPONSE TO ARGUMENTS

2. Examiner acknowledges submission of a declaration under 37 CFR § 1.132 signed by David Rubinsztein, Brinda Ravikumar, and Julie Maidment neé Webb, and the fee filed under 37 CFR § 1.17(i), filed on 11/23/2009.

3. In view of the papers filed 11/23/2009, the inventorship in this nonprovisional application has been changed by the deletion of Julie Webb. The inventorship has been corrected to include David Rubinsztein and Brinda Ravikumar, only.

The application will be forwarded to the Office of Initial Patent Examination (OIPE) for issuance of a corrected filing receipt, and correction of Office records to reflect the inventorship as corrected.

4. Claims 41-51 were rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for clearing intracellular aggregate-prone proteins in the treatment of a protein conformational disorder (PCD) comprising stimulation of autophagy, does not reasonably provide enablement for clearing intracellular aggregate-prone proteins in the

prophylaxis of a protein conformational disorder (PCD). Examiner notes that Claim 42 has been canceled. Applicants traversed this rejection on the grounds that one of ordinary skill in the art would understand the term "prophylactic treatment" to mean a treatment administered before the onset of disease which delays the onset of the disease or reduces the severity of said disease after onset. Applicants provide a definition of "prophylactic" from Webster's Online Dictionary. Applicants point to experiments in the specification indicating that in transgenic mice engineered to develop Huntington's disease (HD), administration of autophagy by CCI-776 delayed the onset of a protein conformational disorder. Thus, Applicants contend that the instant application provides enabling support for "prophylactic treatment" of a protein conformational disorder (PCD). Respectfully, Examiner does not find Applicants' arguments persuasive.

5. "Prevent," "prevention," and "prophylaxis" are potent terms implying that the method of prevention, or a prophylactic agent will necessarily prevent the occurrence of PCD in every patient that receives the treatment at any point following the administration of the prophylactic agent. To this end, neither the Applicants nor the prior art have not demonstrated that the development of PCD can be completely halted in every patient receiving a given pharmacologic intervention (See Kubi and Chauduri or Intelihealth, both already of record). Applicants have demonstrated only that induction of autophagy can delay the onset and/or reduce the severity of a PCD. Therefore, the rejection of Claims 41 and 43-51 under 35 U.S.C. 112, first paragraph, is maintained.

6. Applicants can overcome this rejection by amending the claims to a method of delaying the onset and/or reducing the severity of a PCD.

7. Claims 41-51 were rejected under 35 U.S.C. 112, second paragraph, with respect to the limitation "aggregrate-prone proteins." This rejection is moot in light of Applicants' amendment to Claim 41 and cancellation of Claim 42.

8. Claims 41-51 were rejected under 35 U.S.C. 102(a) as being anticipated by Ravikumar, et al. (Human Molecular Genetics, 2002). Examiner acknowledges Applicants' change of inventorship and declaration indicating that that Ranier Duden is not an inventor of the claimed invention. Therefore Ravikumar, et al., does not qualify as prior art under 35 U.S.C. 102(a), and this rejection is withdrawn.

9. Claims 41-47 and 49-51 were rejected under 35 U.S.C. 102(b) as anticipated by Lin, et al. (European Patent Application Publication no. EP 0 778 023 A1, 1997, provided in IDS). Examiner notes that Claim 42 has been cancelled by Applicants. Applicants traversed this rejection on the grounds that Lin, et al., does not anticipate the claimed invention. Specifically, Applicants contend Lin, et al., teaches treating HD, rather than offering a prophylactic treatment and that insofar as the *in vitro* results disclosed therein can be extrapolated to any *in vivo* situation, they can only be extrapolated to treating of cells after the insult has occurred. Respectfully, Examiner does not find Applicants' arguments persuasive.

10. The amended claims are drawn to a method of clearing intracellular proteins in an individual comprising stimulating autophagy. The limitations "for the prophylactic treatment of a conformational disorder characterized by intracellular aggregation of said proteins" and "wherein said stimulation promotes clearance of said proteins" are considered the intended result of the method. The intended result of a method is not considered to be a patentably distinguishing feature of an invention (MPEP § 2111.04). With respect to the intended result of

prophylactic treatment of a PCD, Applicants may be attempting to define a patient population distinct from patients suffering from HD, as disclosed in Lin, et al. However, Applicants have provided no guidance for the skilled artisan to determine who may be in need of such treatment. Kubi and Chauduri (already of record) teach that HD is diagnosed prior to determination of any abnormalities in the brian (i.e. shrunken areas of the brain). Thus, the art worker would reasonably construe "prophylactic treatment" as reducing the severity of HD, which is tantamount to treating HD, explicitly contemplated in the instant specification, (pg 14, lines 32-36), and taught in Lin, et al. (pg 8, Claim 4).

11. Examiner does not agree with Applicants' assertion that Lin, et al., disclose a treatment protocol. An *in vitro* treatment protocol would involve inducing protein aggregation then administration of rapamycin. Instead, Lin, et al., coincubate cells with rapamycin and glutamate, which induces protein aggregation. In this regard, the cells have not already developed protein aggregates.

12. For the above reasons, the rejection of Claims 41, 43-47, and 49-51 35 U.S.C. 102(b) as anticipated by Lin, et al., is maintained.

13. Claim 48 was rejected under 35 U.S.C. 103(a) as being unpatentable over Lin, et al. (above) in view of the applicant's own admission (see below). Applicants traversed this rejection for the reasons outlined above. Applicants have not disagreed with that the rapamycin analogues of Claim 48 were well-known at the time of filing. Respectfully, Examiner does not find Applicants' arguments persuasive for the reasons discussed above. Therefore, the rejection of Claim 48 under 35 U.S.C. 103(a) as being unpatentable over Lin, et al. (above) in view of the applicant's own admission is maintained.

14. Amended Claims 41 and 43-51 are examined on their merits and the following **FINAL** rejection is made.

Claim Rejections - 35 USC § 112 (1st paragraph)

15. The text of Title 35, U.S.C. § 112, first paragraph can be found in a prior Office action.

16. Claims 41 and 43-51 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The amended claims are drawn to a method of clearing intracellular proteins. The instant specification contains written support for clearing intracellular aggregated proteins but not for clearing any/every intracellular protein.

17. Applicants can overcome this rejection by amending Claim 41 to be a method of clearing intracellular aggregated proteins.

Conclusion

18. Claims 41 and 43-51 remain rejected.

19. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Paul Zarek whose telephone number is (571) 270-5754. The examiner can normally be reached on Monday-Thursday, 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brandon Fetterolf can be reached on (571) 272-2919. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

PEZ

/San-ming Hui/
Primary Examiner, Art Unit 1628